

Appl. No.: 09/554,387
Response dated July 25, 2005
Reply to Office action of January 26, 2005

Remarks:

Claims 11-30 are pending. By way of the present Response, claims 31 and 32, directed to the specified amounts of component a and component b by weight have been added. Basis is provided at page 8, line 7 of the specification.

Applicant notes that the German priority application for this application is in German and that no translation into English has been provided. This will be discussed further below.

The present application is on remand from the Board of Patent Appeals and Interferences (hereinafter "the Board") in its Decision on Appeal (hereinafter "Decision"), which reversed the Examiner's previous rejection of the claims made under 35 USC 103 (a) as lacking basis in law, as argued by Applicant throughout the prosecution and before the Board.

The Board at page 8 of the Decision made note of disclosure in the specification at page 4, lines 13-15 relating to conjugated linoleic acid ("CLA") having low hypocholesteremic action as constituting "acknowledged prior art."

As stated by the Board at page 8:

"Although the record on this point has not been fully developed, nevertheless, it would appear that the foregoing statement (page 4, lines 13 through 15) constitutes acknowledged prior art. In other words, it appears that Applicant would acknowledge that persons having ordinary skill recognized and understood, at the time the invention was made, that conjugated linoleic acid has hypocholesteremic activity. On return of this application to the Examining Corps, the examiner and applicant should clarify if, in fact, that is the case (emphasis added)."

Thus, the Board's recommendation on remand was that the examiner and Applicant "clarify" whether the above-cited disclosure represents acknowledged prior art.

As will be discussed in more detail below, Applicant disagrees that the cited statement constitutes an admission of acknowledged prior art. It is clear from the Board's comments in the Decision and now the Examiner's comments in the Official Action that the disclosure at issue

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has been taken out of context, and that neither the Board then nor the Examiner now has considered the context and meaning of the entire sentence at page 4, lines 13-17.

1) Claim rejections under 35 USC 103

Claims 11-18, 20-27 and 30 are rejected under 35 USC 103 (a) as being unpatentable over Jandacek (3,865,939 of record), Miettinen (EP 0594612B1 of record) and Hasegawa (English translation of record) in view of Lee et al. ("Conjugated Linoleic Acid and Atherosclerosis in Rabbits") or Applicant's "admission" in the specification at page 4, lines 13-15.

The rejection is respectfully traversed.

The combined teachings of Jandacek, Miettinen and Hasegawa have been discussed at length both during the prosecution and before the Board. According to the Board at pages 3 and 4 of the Decision, the "examiner has not established that the relatively broad disclosures of Jandacek or Miettinen would have led a person having ordinary skill in the art to applicant's claimed subject matter..."

With respect to the teachings of Hasegawa, the Board, citing the holding in Grabiak, stated at page 6 that "the examiner in this appeal does not cite any reference disclosing the art-recognized equivalence of linoleic acid and conjugated linoleic acid for the purpose of achieving a cholesterol lowering effect. In the absence of prior art disclosing such art-recognized equivalence, there is inadequate support for the PTO's position that this modification would have been prima facie obvious."

At page 5 of the Official Action, the Examiner admits that "[T]he cited prior art herein does not expressly disclose the employment of conjugated linoleic acid (CLA)...in combination with a phytosterol or phytosterol esters (emphasis in original)" in the claimed invention.

To address the deficiencies of the combined teachings of the primary references, the

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Examiner now cites Lee or Applicant's alleged "admission" in the specification at page 4, lines 13-15 for the proposition that, at the time of Applicant's invention, it was known in the art that CLA reduced cholesterol.

It is respectfully submitted that neither Lee nor the cited disclosure in Applicant's specification support the Examiner's position that, at the time of the invention, it was known that CLA reduced cholesterol.

With respect to Lee, Applicant notes that the Lee reference is cited in US Pat. No. 5,837,733 ("Pariza") at Col. 1, lls. 30-35. At Col. 1, lls. 37-45 of Pariza, the teachings of Nicolosi and Laitinen are also cited with respect to their studies on the effect of CLA and lowering cholesterol. Nicolosi and Laitinen reported in their publication in FASEB that:

"conjugated linoleic acid [CLA] had insignificant effect on plasma lipids and lipoprotein cholesterol, but did bring about a significant 45% reduction in aortic fatty streak formation after feeding to hamsters (emphasis supplied)..."

Thus, Nicolosi and Laitinen reported that CLA had **no effect** on cholesterol level. The teachings of Nicolosi and Laitinen are thus totally contrary to that of the Lee reference as to the lowering effect of CLA on cholesterol.

As to what one of ordinary skill then would have appreciated and known, at the time of Applicant's invention, with respect to the effect of CLA on cholesterol, it is submitted that it was not known and not at all settled in the scientific community as to what effect CLA actually had on lowering serum cholesterol in light of the conflicting scientific evidence discussed above.

In a Court of Law, the Examiner would thus fail to meet the "preponderance of the evidence" standard in showing that, at the time of the invention, one of skill in the art would have known that CLA lowered cholesterol, based on the directly contrary findings of Lee and Nicolosi.

As for Applicant's alleged "admission" at page 4 of the specification, which is being used as an alternative basis for this rejection, it is submitted that the cited disclosure has been read **out of context and clearly not read in its entirety** by both the Board and the Examiner.

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The disclosure at issue is at page 4, lines 13-17, and states:

"It is known of conjugated linoleic acid that it has a low hypocholesteremic action; [but] its use in foodstuffs or as a foodstuff supplement, however, is attributed to the fact that it assists the combustion of endogenous fats (emphasis added)."

According to this disclosure, CLA, when used in foodstuffs or foodstuff supplements, aids in the combustion of fats, and thus is operating by some other mechanism than lowering serum cholesterol. The specification does not state that its use in foodstuffs or foodstuff supplements was known to lower serum cholesterol. In fact, it states that CLA assists in the combustion of endogenous fats in foodstuffs and foodstuff supplements.

Neither the Board nor the Examiner has considered this disclosure in its entirety. It clearly does not represent an admission that it was known or acknowledged in the art, at the time of Applicant's invention, that CLA lowered serum cholesterol, as stated by the Examiner in the present rejection.

It is therefore respectfully submitted that there is no legal basis for the rejection under 35 USC 103(a) in relation to the Examiner's statement at page 6 of the Action that "one of ordinary skill in the art would have reasonably expected that combining CLA and phytostenol or of phytostenol esters of a fatty acid herein, all known useful for the same purpose in a composition to be administered would improve the therapeutic effect of reducing serum cholesterol content in a mammal (emphasis in original)."

Neither the scientific evidence at the time of the invention nor Applicant's alleged admission support this position. Therefore, the holding in *In re Kerkoven* is inapplicable to the particular facts in issue here.

With respect to the Examiner's comments relating to Miettinen and/or Hasegawa providing the "motivation for the combination of phytostenol or its esters and fatty acids **broadly** including conjugated linoleic acid... (emphasis added)", the Board in its Decision, as discussed above, rejected this argument and reasoning. To continue to use such legally defective reasoning

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now is still in error and would clearly again be rejected by the Board.

It is therefore respectfully submitted that claims 11-18, 20-27 and 30 are patentable over the prior art. Claims 31 and 32, newly added, are also patentable over the prior art, as there is no teaching or suggestion in the prior art of the specified amounts of components a and b, as called for by these claims. The Examiner is kindly requested to reconsider and withdraw the rejection.

Claims 19, 28-29 are rejected under 35 USC 103 (a) as being unpatentable over Jandacek, Miettinen and Hasegawa in view of Lee or "Applicant's admission" as applied to claims 11-18, 20-27 and 30, further in view of Hidevgy (US 5,277,910 of record).

The rejection is respectfully traversed.

Applicant has already addressed the rejection of claims 11-18, 20-27 and 30 in detail above as to why that rejection is without legal basis and does not constitute a *prima facie* case of obviousness.

Hence, the present rejection, which is further in view of the previously rebutted rejection can not stand.

It is therefore respectfully submitted that claims 19, 28-29 and newly added claims 31 and 32 are patentable over the prior art.

The Examiner is kindly requested to reconsider and withdraw the rejection.

Claims 11-30 are rejected under 35 USC 103(a) as being unpatentable over Jandacek, Miettinen and Hasegawa in view of US Pat. No.5,837,733 ("Pariza"), further in view of Hidevgy.

The rejection is respectfully traversed.

With respect to Pariza, Applicant notes that its 102 (e) prior art date is February 26, 1997. Applicant's foreign priority application was filed November 14, 1997, which is less than one year after the US filing date of Pariza above.

Applicant expressly reserves the right, without prejudice, to submit a Declaration under

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37 CFR 1.131 to remove Pariza as a reference.

Such a Declaration would require the translation of the German priority application and notebook records pertaining to the claimed invention into English, which will require some time. Should Applicant pursue this course, the Examiner is kindly requested to consider the Declaration.

Pariza is cited by the Examiner as a secondary reference for its teachings that "CLA significantly lowers or reduces much more serum apolipoprotein B secretion in animals than linoleic acid (LA) does according to the testing results therein (see Fig. 1, col. 2, line 34-37... (emphasis in original)."

According to the Examiner, it would have been obvious at the time the invention was made to employ CLA in lieu of LA in the claimed invention, "since CLA is known to be much more effective than LA in reducing serum "bad" cholesterol through reducing apolipoprotein B secretion in animals." And that one of skill would have reasonably expected that combining (emphasis in original) CLA and a phytosterol would improve the therapeutic effect for reducing serum cholesterol content in a mammal in view of the holding *In re Kerkhoven*.

According to the Examiner, "[F]urther, the motivation for the combination (emphasis in original) of phytosterol esters and fatty acids **broadly including linoleic acid and also including conjugated linoleic acid** (emphasis added), employed in the instant claimed method, has been provided by Miettinen et al. and/or Hasegawa et al. respectively."

The Examiner's attention is again directed to pages 4-6 of the Decision with respect to the Board's reversal of the Examiner's rejection based on the teachings of Jandacek, Miettinen and Hasagawa, which are again the primary references of the present rejection.

As evidenced at these pages of the Decision, the Board took issue with the Examiner's statements relating to the "broad" teachings of the prior art.

At page 4, 1st full paragraph, the Board stated:

"By the same token, the examiner argues that Miettinen suggests 'the combination of

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phytostenol esters and fatty acids broadly including linoleic acid, employed in the instant claimed method...(emphasis in original). However, the examiner has not established that the relatively broad disclosures of Jandacek or Miettinen would have led a person having ordinary skill in the art to applicant's claimed subject matter requiring conjugated fatty acids... (emphasis added)."

At page 5 of the Decision with respect to Hasegawa, the Board stated:

"Second, according to the Examiner, Hasegawa discloses that an excellent cholesterol decreasing effect was obtained through the synergistic action between linoleic acid and sitostenol... According to the Examiner, 'one of skill in the art would clearly recognize that the known structure of linoleic acid is substantially similar to the structure of conjugated linoleic acid because they are structural isomers which have two double bonds but merely differ in one position of one double bond..'

In other words, the examiner argues that the cited references [Jandacek, Miettinen and Hasagawa] would have led a person having ordinary skill in the art to a hypocholesteremic preparation comprising sitostenol and linoleic acid; that linoleic is 'substantially similar' in structure compared with conjugated linoleic acid; and, accordingly, that the cited references would have led a person having ordinary skill in the art to a hypocholesteremic preparation comprising sitostenol and conjugated linoleic acid. We disagree (emphasis added)."

At page 6, second full paragraph, the Board further states:

"Like the situation presented in Grabiak, the examiner in this (emphasis in original) appeal does not cite any reference disclosing the art-recognized equivalence of linoleic acid and conjugated linoleic acid for the purpose of achieving a cholesterol lowering effect. In the absence of prior art disclosing such art-recognized equivalence, there is inadequate support for the PTO's position that this modification would have been prima facie obvious (emphasis added)...The legal conclusion of obviousness must be supported by facts. Where the legal conclusion is not supported by facts it cannot stand (emphasis in original)."

The Examiner's statement at page 9, 3rd paragraph that the motivation to combine phytostenol esters and fatty acids "broadly including linoleic acid and also including conjugated linoleic acid...has been provided by Miettinen et al. and /or Hasegawa et al." was clearly rejected by the Board of Appeals (emphasis added). The Board stated that the Examiner was required to present prior art which disclosed the "art-recognized equivalence" of linoleic acid and CLA.

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To force Applicant to re-litigate this matter before the Board, which has already clearly rejected the Examiner's position, which she has repeated here in this rejection, would be an unnecessary waste of the Board's and Applicant's valuable time and money.

Furthermore, Pariza discloses that CLA and linoleic acid are clearly not "art-recognized equivalents", as has been argued by the Examiner, since CLA was significantly more effective in reducing apolipoprotein B than was linoleic acid.

The Examiner's "motivation for the combination of phytosterol esters and fatty acids broadly including linoleic acid and also including conjugated linoleic acid" is based on the teaching of the primary references. This alleged "motivation" is clearly lacking and in error, as pointed out by her own Board of Appeals, as discussed at length above.

The rejection of claims 11-30 over Jandacek, Miettinen and Hasegawa in view of Pariza and further in view of Hidvegi is clearly improper and the Examiner is kindly requested to withdraw the rejection.

Since the Board did not need to consider Applicant's evidence of non-obviousness presented on Appeal because the Board held that the Examiner had failed to establish a *prima facie* case of obviousness, Applicant is now re-entering the evidence presented on Appeal into the record of the remanded application for consideration on the merits and for the purposes of a complete record.

2) Indicia of Non-Obviousness

A. Applicant's Showing of Significantly Improved Results

Finally, even if it were assumed, for argument's sake, that a *prima facie* case of obviousness could be established based upon the cited references, which it cannot, any such alleged *prima facie* case of obviousness would be overcome by Applicant's showing of synergism between the phytosterol(ester)s and the conjugated fatty acids and the unexpected,

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significantly improved results of the claimed preparations compared to the prior art.

Applicant respectfully submits that the combination of phytostenol(ester)s and conjugated fatty acids in accordance with Applicant's invention perform better than either component alone in reducing serum cholesterol levels. This is clearly evidenced by the Examples set forth in Applicant's Specification, beginning at page 8, line 17. As can be seen from Table 1, at page 9, the combinations decrease the serum cholesterol levels in amounts greater than either component alone. The Examiner has argued that the data shows less than additive therapeutic effects. **APPLICANT RESPECTFULLY SUBMITS THAT THE EXAMINER IS INCORRECT.** Example C5 shows the effect of 10% by weight of conjugated linoleic acid alone. After 48 hours, the "% rel." of radio-labeled cholesterol is 60% (a greater decrease from 100% is BETTER). Example C1 shows the effect of 10% by weight of β -sitostenol alone. After 48 hours, the "% rel." of radio-labeled cholesterol is 35%. **HOWEVER**, as shown in Example 1, half the amount of β -sitostenol (5% by weight) and half the amount of conjugated linoleic acid (5% by weight), in combination, result in a "% rel." of radio-labeled cholesterol of 23%. The Examiner is incorrect to argue that because Example C5 results in a 40% decrease, and Example C1 results in a 65% decrease, that the 77% decrease of Example 1 is less than additive. Such logic would require a relative reduction of greater than 105%. Additionally, as mentioned previously, as is the case with most "purifications" or "removals", the removal of each additional amount of an undesired impurity (*i.e.*, cholesterol) is progressively more difficult.

Applicant submits that a 77% relative reduction using half the amounts of a phytostenol and a conjugated fatty acid, compared to a 40% relative reduction and a 65% relative reduction using twice the amount of either material alone, is evidence of both a synergistic effect associated with the combination and a significant improvement over prior art hypocholesteremic preparations.

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This significant improvement is surprising as noted in the Specification.

Applicant's Specification specifically states:

"Surprisingly, it has been found that mixtures of phytosterols or phytosterol esters with conjugated fatty acids or fatty acid glycerides synergistically cause the reduction of the cholesterol content in the blood serum."
(See, Applicant's Specification, page 2, lines 25-29).

It is submitted that Applicant's showing of synergism and unexpected and improved results sufficiently rebuts any alleged *prima facie* case of obviousness.

B. Examiner's Rebuttal in Paper Nos. 16 & 19

In Paper No. 16, the Examiner argued "that lauric acid in lauric acid β -sitostanol ester or lauric acid β -sitostenol ester employed in the testing herein is not even an unsaturated carboxylic acid, which is not a conjugated fatty acid [and t]hus, these two compounds are not within the scope of the claimed invention" (See, Paper No. 16, page 4). Based upon this argument, the Examiner had contended that the results shown for the combination of a lauric acid ester of β -sitostenol or β -sitostanol and conjugated linoleic acid "[are] not deemed relevant." (See, *id.*).

Applicant brought to the Examiner's attention the fact that the lauric acid sitostenol esters listed in Table 1 are **phytosterol esters** and their combination as a mixture with conjugated linoleic acid is most certainly within the scope of the present invention.

In Paper No. 19, the Examiner argued that Applicant had presented no side-by-side comparison with the prior art.

On these bases, the Examiner's position was that Applicant's showing was insufficient.

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C. Law Pertaining to Indicia of Non-Obviousness

To begin with, the Federal Circuit has held that "the PTO must consider comparative data in the specification in determining whether the claimed invention provides unexpected results." (*In re Soni*, 34 USPQ.2d 1684, 1687 (Fed. Cir. 1995), citing *In re Margolis*, 228 USPQ 940 (Fed. Cir. 1986)). The Federal Circuit also held that, "when an applicant demonstrates *substantially* improved results, . . . , and states that the results were *unexpected*, this should suffice to establish unexpected results *in the absence of evidence to the contrary*." (*Soni*, at 1688 (*emphasis in original*)).

Secondly, with respect to the type of showing necessary, Applicant respectfully submits, that Section 716 of the M.P.E.P. does not require the submission of a "side-by-side" comparison in order to successfully establish unexpected results. Applicant respectfully submits, that section 716.02(e) simply outlines one requirement of a Declaration under 37 C.F.R. §1.132, namely that such a Declaration compare the claimed subject matter with the closest prior art available. There is no requirement for a Declaration.

However, section 716.02(b), which is more specifically related to the burden of proof concerning allegations of unexpected results, clearly indicates that both direct and *indirect* comparisons with the prior art may be made.

D. Sufficiency of Applicant's Showing

Regardless of the correctness of the Examiner's contention that §716.02(e) of the M.P.E.P. requires a side-by-side comparison, and contrary to the Examiner's assertion that Applicant failed to set forth a side-by-side comparison, Applicant respectfully submits that the comparative data set forth in the Specification is a sufficient comparison of the invention and the closest prior art available.

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Specifically, Applicant compares combinations of a phytostenol(ester) component and a conjugated fatty acid component (Examples 1-5) with either a phytostenol(ester) component or a conjugated fatty acid component (Comparative Examples C1-C5).

Thus, Applicant specifically submits that the comparative data most certainly compares the claimed mixtures with the prior art components. Furthermore, the comparative data need not be present in the form of a Declaration. Data set forth in the Specification must be considered. Finally, the significant improvement shown in the Examples is identified in the Specification as being unexpected.

Accordingly, it is submitted that Applicant's showing of synergism and unexpected and improved results sufficiently rebuts any alleged *prima facie* case of obviousness. Applicant submits that significantly improved results shown by direct comparison, as set forth in the Specification, along with Applicant's statement that such improved results are unexpected, satisfy the required burden under Section 716.02(b) of the M.P.E.P. and *Soni*, absent evidence to the contrary.

For all of the reasons provided above, it is respectfully submitted that claims 11-32 of the present application are patentable over the prior art. Favorable reconsideration and an early Notice of Allowance are therefore respectfully solicited.

Respectfully submitted,


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